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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,840	01/28/2002	Patrick Soon-Shiong	ABI1550-1	7072

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EXAMINER	
DELACROIX MUIRHEI, CYBILLE	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 05/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,840	SOON-SHIONG ET AL.	
	Examiner	Art Unit	
	Cybille Delacroix-Muirheid	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *05/12/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

The following is responsive to Applicant's election received Jan. 22, 2004.

Applicant's election of chemotherapeutic drugs as the therapeutic agent with traverse is acknowledged. The traversal is on the grounds that a thorough search of the claims directed to methods for treating a subject having an infirmity by administering a sub-therapeutic dose level of a pharmacologically active agent such as a chemotherapeutic agent would necessarily include a search of agents such as taxanes, anti-neoplastics, etc. Furthermore, a thorough search of the claims employing various routes of administration would necessarily include a search of several possible alternative modes of administration.

Said arguments have been considered and have been found to be persuasive in part. The election requirement for a specific mode of administration is withdrawn. However, the Examiner respectfully maintains the requirement for a species of active agent. The claimed active agents are structurally and chemically distinct and are used to treat different types of diseases. Therefore, the search for one method, e.g. treating cancer by administering a sub-therapeutic dose of a chemotherapeutic drug, would not be required for a search of a method for treating depression by administering a sub-therapeutic dose of an anti-depressant.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

Applicant's Information Disclosure Statement received May 12, 2003 has been considered. Please refer to Applicant's copy of the 1449 submitted herewith.

Abstract

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Objection(s)

1. Claim 17 is objected to because of the following informalities: at lines 5-6, the use of the phrase "(i.e. via suppository),...(i.e. via pessary)" is improper. These phrases should be deleted from the claim. Appropriate correction is required.

Claim Rejection(s)—35 USC 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for sub-therapeutic administration of paclitaxel in the treatment of paclitaxel responsive cancers, does not reasonably provide enablement for the treatment of all types of cancer ('infirmity") using any chemotherapeutic active agent. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

3. The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of

the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The claims are drawn to a method for treating " an infirmity",i.e. cancer, in a patient by administering a sub-therapeutic dose of a chemotherapeutic agent.

(2) The state of the prior art

With respect to the term "cancer", this a broad term which encompasses numerous forms of cancerous diseases, each involving different types of tissues and organs. As recognized in the art, many different antineoplastic drugs are used to treat a variety of cancers. Please see Goodman & Gilman's pages 1227-1229.

(3) The relative skill of those in the art

The relative skill of those in the art is high.

(4) The predictability or unpredictability of the art

The unpredictability of the pharmaceutical and chemical art is high.

(5) The breadth of the claims

The claims are very broad and encompass treatment of numerous types of cancer by administering a sub-therapeutic dose of any chemotherapeutic agent, which differs chemically and structurally.

(6) The amount of direction or guidance presented

Applicant's specification does not provide guidance for the treatment of all types of cancers using any "chemotherapeutic agent." The specification provides no guidance to enable one of ordinary skill in the art to use the invention commensurate in scope with the claims, which, as stated above, are broad and encompass numerous cancerous diseases and compounds, which differ chemically and structurally. In re Dreshfield, 110 F.2d 235, 45 USPQ 36 (CCPA 1940), gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result." Applicant's specification does not set forth a representative number of examples of compounds capable of carrying out the claimed methods. Applicant's specification appears to only be enabled for the treatment of cancers responsive to paclitaxel (please see page 18, Example 1). Otherwise, Applicant has not set forth a representative number of examples of cancers and chemotherapeutic compounds, which would be capable of treating various cancers when administered at a sub-therapeutic dose. Therefore, Applicant's Example pertaining to paclitaxel and cancers responsive to paclitaxel is not representative of the huge scope of compounds and cancers encompassed by the claims.

(7) The presence or absence of working examples

The only working example in the specification involves the description of a regimen for treating cancers responsive to the administration of paclitaxel.

(8) The quantity of experimentation necessary

Since (1) the art establishes that there are numerous forms of cancer treatable by many different anti-neoplastic agents; (2) since the claims are broad and require the treatment of numerous types of cancer by the administration of any chemotherapeutic agent, (3) since Applicant's specification does not provide a representative number of cancers and compounds which can be used in the claimed method, and (4) since compound structure and activity for pharmaceutical use must be determined from case to case by painstaking experimental study, one of ordinary skill in the art would be burdened with undue experimentation to determine the chemotherapeutic compounds and sub-therapeutic dosages that would be capable of treating the large number of cancerous disorders encompassed by the claims.

Claim Rejection(s)—35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-4, 9-12, 14-17, 18-21 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 9406422 ('422).

WO '422 discloses a method of administering for a long term, low doses of paclitaxel to a patient suffering from cancer (breast, lymphoma). The method specifically requires administering as a 96-hour continuous infusion a dose level of paclitaxel containing between 70 and 140 mg/M^2. The paclitaxel solution is delivered through a permanent central intravenous catheter, with cycles repeated every 21 days. WO '422 additionally teaches that the administration of low dose paclitaxel results in less adverse side effects and reduces the chance of a patient developing mdr paclitaxel resistance. Please see the abstract; page 5, lines 1-24; page 7, lines 4-26; page 9, lines 3-6.

WO '422 also discloses a composition comprising a final infusion solution prepared by diluting the total daily paclitaxel dose in 250 or 500 ml of 5% dextrose injection, USP or 0.9% sodium chloride injection USP in a glass, polyolefin or polypropylene container. Please see page 7, lines 4-9.

5. Claims 1-4, 6-10, 11, 13-14, 15-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Regazzoni et al.

Regazzoni et al teach a method for treating patients with metastatic breast cancer, the method comprising administering to the patients low-dose continuous infusion (250 mg/M^2 for 21 days) of 5-fluorouracil. Regazzoni et al. additionally teach that all patients who received the low-dose continuous infusion felt that the treatment was easy to tolerate. Please see the abstract.

Claim Rejection(s)—35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 5-8 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO '422, supra.

WO '422 as applied above.

However, WO '422 does not disclose local administration of paclitaxel, nor does WO '422 teach the claimed length of treatment. However, one of ordinary skill in the art would reasonably expect local administration to be effective in delivering paclitaxel to

the tumor or cancer to be treated. Moreover, since the length of treatment is related to the efficacy of the overall efficacy, it would have been obvious to one of ordinary skill in the art at the time the invention was made to further modify the length of treatment in WO '422 such that therapeutic levels of paclitaxel are achieved without the undesirable side effects.

7. Claims 5 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Regazzoni et al. in view of WO '422, supra.

Regazzoni et al. as applied above.

However, Regazzoni et al. do not disclose local administration of 5-fluorouracil. However, one of ordinary skill in the art would reasonably expect local administration to be effective in delivering 5-fluorouracil to the tumor to be treated. Furthermore, Regazzoni et al. do not disclose the use of paclitaxel in the low-dose continuous infusion treatment of breast cancer. Yet, the Examiner refers to WO '422, which discloses treatment of breast cancer by administering paclitaxel for a long term at a low-dose.

Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Regazzoni et al. by using low dose continuous infusion of paclitaxel because, based on the desirable teachings of WO '422, one of ordinary skill in the art would reasonably expect low dose, long term treatment with paclitaxel to be equally effective in treating the breast cancer patients of Regazzoni et al.

Conclusion

Claims 1-21 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cybille Delacroix-Muirheid whose telephone number is 571-272-0572. The examiner can normally be reached on Mon-Fri from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached at 571-272-0584. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CDM

May 24, 2004

Cybille Delacroix-Muirheid
Patent Examiner Group 1600